Regional cerebral blood flow changes in patients with internet addiction

Dear Editor,
Internet addiction (IA) has become a severe challenge of our modern world today, though little is known about its pathology.

In this context, the interesting study by Liu et al. in the May-August 2016 issue of HJNM using ^{99m}Tc-labelled ethylene biyldicysteinate dimer single photon emission tomography (SPET) at rest and after pharmaceutical (adenosine) stress is more than welcomed [1]. As this seems to be the first perfusion SPET study in this indication, the obtained data may be discussed carefully.

There are mainly the following questions: a) Regional cerebral blood flow (rCBF): There is no description on how the rCBF was calculated: Was it scaled relatively to the whole brain mean value or to the cerebellar mean value? b) P value threshold and clusters: There is no indication of whether the authors are performing any kind of correction for multiple comparisons in the statistical parametric mapping (SPM) t-test. This, combined with the use of a really "liberal" voxel P value of only 0.01 could be subject to providing many false positive results. Generally a P value threshold of 0.001 should be used. In addition, there is no information related to the clusters. For the question of the validity of parametric statistical methods used for the analysis of functional neuro-imaging data, we would like to mention the important recent paper by Eklund et al. 2016 [2]. c) Data analysis: The authors state (p. 97): "*As some abnormal rCBF in adenosine-stressed state might relate with normal responses to adenosine compared to resting state, we excluded those regions that showed abnormal rCBF in stressed state in healthy controls (Table 4) from those in IA group (Table 5). The rest abnormal regions were compared between the IA group and the control group*". For this, with SPM a flexible factorial design with all the data rather than only t-tests would have been interesting to find out whether the difference between the groups at stress is the same difference observed between the groups at rest. In "traditional" region-of-interest statistics, a repeated 2-way ANOVA to account for individual variance would have been done. The authors are, however, just "manually" removing the regions that pop-up in the previous analysis. *In conclusion*, it would be of great scientific interest if the authors of this first SPET study on an important indication, IA, could give us some more details on their data.

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The author declares that he has no conflicts of interest

Bibliography

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Authors' reply

To the comments of Prof. Andreas Otte to our work [1] we reply as follows: As was mentioned by Prof. Andreas Otte, our study was the first study of regional cerebral blood flow changes in patients with internet addiction. Therefore, there was not much previous, established experience to refer to. As an exploration study, it was inevitable that there were some insufficiencies. We feel great appreciation to Prof. Andreas Otte for his comments on our work, which will improve our studying quality in this field in the future.

Prof. Andreas Otte inquired in his letter how the regional cerebral blood flow (rCBF) was calculated, and was scaled, relatively to the whole brain mean value or to the cerebellar mean value. All rCBF data were scaled relatively to the whole brain, in our study. As for the question in relation to the test level, the P-value of 0.05 was only used when comparing intergroup differences of baseline or clinical information of patients using SPSS, while the P-value of 0.01 was used for the statistical parametric mapping (SPM) t-test. We had tried using the test level of P<0.001 to indicate the significance when performing the SPM t-test, but there were not very meaningful findings identified at this test level. This might be explained by the relatively old generation and low sensitivity of the SPET scanner used in our study. For the purpose to identify more potential cerebral regions with abnormal rCBF, we lowered down the test level to 0.01, although this might had resulted in some false-positive results. However, in order to control false-positive errors, we performed intragroup comparisons from rest to adenosine-stressed status firstly by paired t test to identify cerebral regions with obvi-

ous rCBF changes because of administration of adenosine. On the basis of these cerebral regions, we subsequently performed a two-sample t test to compare intergroup differences to identify cerebral regions with rCBF that could have attributed to internet addiction. We believed that this "two-step" statistical mode might reduce the probability of false-positive results to some extent. As for the cluster question in relation to SPM analysis, it seems more problematic and more prone for clusterwise inference to produce false-positive results than voxelwise inference, as mentioned in the paper by Eklund et al (2016) [2]. We did not take the two-way ANOVA analysis, instead, we performed the more suitable "two-step" statistical mode mentioned above. However, when facing multiple comparisons, we did adjust the P-values with the relatively conservative Bonferroni method.

Thanks again for the interesting and the meaningful comments of Prof. Andreas Otte to our study. If there are any more queries, please do not hesitate to contact us.

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